

No new matter has been introduced.

REMARKS

Claims 1 and 6 are amended herewith to remove the limitation introduced with Applicants' Preliminary Amendment of December 3, 2001, after reviewing the issued restriction requirement (Paper No. 6) and having a telephone conference with Supervisory Patent Examiner Joseph McKane on this date. Therefore, the claims pending are identical to the claims as originally filed on August 28, 2001.

In response to the Restriction Requirement (Paper No. 6) issued June 5, 2002, Applicants hereby elect the invention of Group IV (Compounds of Formula I which contain "carboxamide"). In addition, applicants elect "rheumatoid arthritis" as the inflammatory disease and compound no. 75 (see Table A, page 31 of the specification) as the compound of choice, for further prosecution on the merits. It is believed that the elected species are readable on claims 1-9, and 13-15.

If the Examiner has any questions and believes that a telephone conference with Applicants' representative would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at (617) 720-3500 (Extension 286).

Respectfully submitted,

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MARKED-UP CLAIMS

1. (Twice Amended) A method for inhibiting unwanted cellular proliferation associated with an inflammatory disease, said method comprising the step of contacting a cell the proliferation of which contributes to inflammation *in situ* with an effective amount of  
a compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

$n$  is 0, 1, 2, 3 or 4;

$X$  is absent,  $(\text{C}_1\text{-C}_3)$  alkyl,  $(\text{C}_1\text{-C}_3)$  alkenyl, or  $(\text{C}_1\text{-C}_3)$  alkynyl;

$Y$  is C, N, P, Si or Ge;

$R_1$  is absent, -halo, -R, -OR, -SR, -NR<sub>2</sub>, -ONR<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R, -C(S)R, -C(O)OR, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NR<sub>2</sub>, -C(S)NR<sub>2</sub>, -C(O)NR(OR), -C(S)NR(OR), -C(O)NR(SR), -C(S)NR(SR), -CH(CN)<sub>2</sub>, -CH[C(O)R]<sub>2</sub>, -CH[C(S)R]<sub>2</sub>, -CH[C(O)OR]<sub>2</sub>, -CH[C(S)OR]<sub>2</sub>, -CH[C(O)SR]<sub>2</sub>, -CH[C(S)SR]<sub>2</sub> or aryl;

$\text{Ar}_1$  is aryl, substituted aryl, heteroaryl other than imidazole, nitroimidazole and triazole, heteroarylium other than imidazolium, nitroimidazolium and triazolium,  $(\text{C}_5\text{-C}_8)$  cycloalkyl or  $(\text{C}_5\text{-C}_8)$  heterocycloalkyl;

$\text{Ar}_2$  is aryl or substituted aryl;

$\text{Ar}_3$  is aryl, substituted aryl, biaryl or heteroaryl other than imidazole, nitroimidazole and triazole;

each R is independently selected from the group consisting of -H,  $(\text{C}_1\text{-C}_6)$  alkyl, substituted  $(\text{C}_1\text{-C}_6)$  alkyl,  $(\text{C}_1\text{-C}_6)$  alkenyl, substituted  $(\text{C}_1\text{-C}_6)$  alkenyl  $(\text{C}_1\text{-C}_6)$  alkynyl, substituted  $(\text{C}_1\text{-C}_6)$  alkynyl, and  $(\text{C}_1\text{-C}_6)$  alkoxy;

the aryl substituents are each independently selected from the group consisting of -halo, trihalomethyl, -R, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR' and -C(S)SR';

the alkyl, alkenyl and alkynyl substituents are each independently selected from the group consisting of -halo, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', aryl,  $\gamma$ -butyrolactonyl, pyrrolidinyl and succinic anhydridyl; and

each R' is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl and (C<sub>1</sub>-C<sub>6</sub>) alkynyl [,wherein thiophene is the only heterocyclic substituent].

6. (Twice Amended) A method of treating an inflammatory disease, said method comprising the step of administering to a subject suffering from an inflammatory disease a therapeutically effective amount of a compound having the formula:



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

n is 0, 1, 2, 3 or 4;

X is absent, (C<sub>1</sub>-C<sub>3</sub>) alkyl, (C<sub>1</sub>-C<sub>3</sub>) alkenyl, or (C<sub>1</sub>-C<sub>3</sub>) alkynyl;

Y is C, N, P, Si or Ge;

R<sub>1</sub> is absent, -halo, -R, -OR, -SR, -NR<sub>2</sub>, -ONR<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R, -C(S)R, -C(O)OR, -C(S)OR, -C(O)SR, -C(S)SR, -C(O)NR<sub>2</sub>, -C(S)NR<sub>2</sub>, -C(O)NR(OR), -C(S)NR(OR), -C(O)NR(SR), -C(S)NR(SR), -CH(CN)<sub>2</sub>, -CH[C(O)R]<sub>2</sub>, -CH[C(S)R]<sub>2</sub>, -CH[C(O)OR]<sub>2</sub>, -CH[C(S)OR]<sub>2</sub>, -CH[C(O)SR]<sub>2</sub>, -CH[C(S)SR]<sub>2</sub> or aryl;

Ar<sub>1</sub> is aryl, substituted aryl, heteroaryl other than imidazole, nitroimidazole and triazole, heteroarylium other than imidazolium, nitroimidazolium and triazolium, (C<sub>5</sub>-C<sub>8</sub>) cycloalkyl or (C<sub>5</sub>-C<sub>8</sub>) heterocycloalkyl;

Ar<sub>2</sub> is aryl or substituted aryl;

Ar<sub>3</sub> is aryl, substituted aryl, biaryl or heteroaryl other than imidazole, nitroimidazole and triazole;

each R is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkenyl (C<sub>1</sub>-C<sub>6</sub>) alkynyl, substituted (C<sub>1</sub>-C<sub>6</sub>) alkynyl, and (C<sub>1</sub>-C<sub>6</sub>) alkoxy;

the aryl substituents are each independently selected from the group consisting of -halo, trihalomethyl, -R, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR' and -C(S)SR';

the alkyl, alkenyl and alkynyl substituents are each independently selected from the group consisting of -halo, -R', -OR', -SR', NR'<sub>2</sub>, -NO<sub>2</sub>, -CN, -C(O)R', -C(S)R', -C(O)OR', -C(S)OR', -C(O)SR', -C(S)SR', aryl, γ-butyrolactonyl, pyrrolidinyl and succinic anhydridyl; and

each R' is independently selected from the group consisting of -H, (C<sub>1</sub>-C<sub>6</sub>) alkyl, (C<sub>1</sub>-C<sub>6</sub>) alkenyl and (C<sub>1</sub>-C<sub>6</sub>) alkynyl [, and wherein thiophene is the only heterocyclic substituent].